

## New Syntheses on the Basis of 4-Hydroxy-2*H*-chromen-2-ones

A. A. Avetisyan, A. G. Alvandzhyan, and K. S. Avetisyan

Erevan State University, ul. A.Manukyana 1, Erevan, 375025 Armenia  
e-mail: organkim@sun.ysu.am

Received January 25, 2008

**Abstract**—Alkylation of 4-hydroxy-2*H*-chromen-2-ones with 2-chloromethyloxirane in acetone in the presence of potassium carbonate gave 4-(2,3-epoxypropoxy)-2*H*-chromen-2-ones which were treated with various amines to obtain the corresponding 4-(3-amino-2-hydroxypropoxy)-2*H*-chromen-2-ones, and the latter were acylated at the hydroxy group with benzoyl chloride.

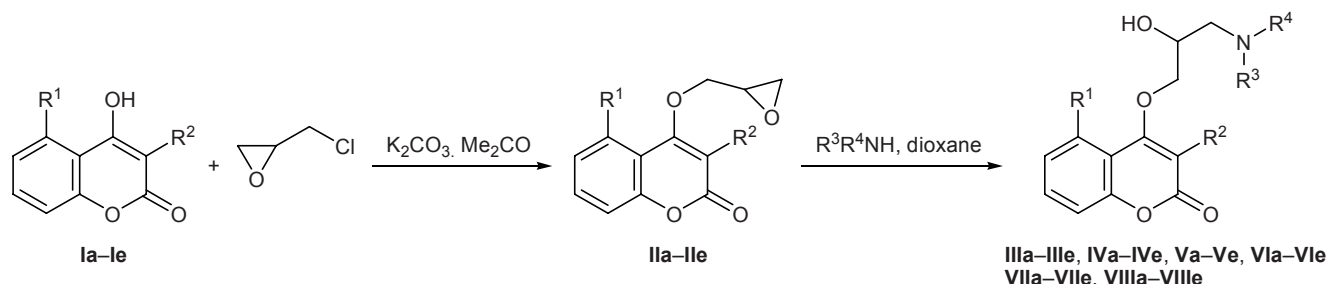
**DOI:** 10.1134/S1070428009070161

In continuation of our studies in the field of synthesis of new O-alkyl derivatives of chromenes [1], in the present work we performed alkylation of 4-hydroxy-2*H*-chromen-2-ones **Ia–Ie** with 2-chloromethyloxirane. Effects of various factors on the process were studied, and optimal reaction conditions were developed. 4-(2,3-Epoxypropoxy)-2*H*-chromen-2-ones **Ila–Ile** were synthesized by heating compounds **Ia–Ie** with chloromethyloxirane at a ratio of 1 : 1.5 in anhydrous

acetone in the presence of potassium carbonate (Scheme 1). The product structure was confirmed by elemental analyses and IR and NMR spectra.

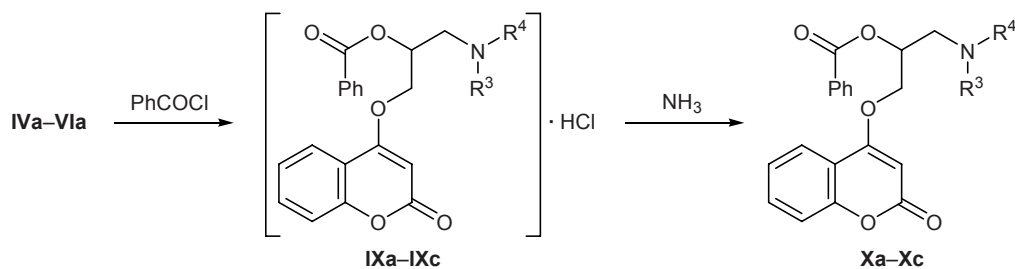
It is known that reactions of epoxy derivatives with amines underlie convenient procedures for the preparation of amino alcohols which are used as intermediate products in syntheses of natural and biologically active organic compounds [2–8]. Various vicinal amino alcohols and their derivatives functionalized at the hydroxy

Scheme 1.



$R^1 = R^2 = H$  (**a**);  $R^1 = Me, R^2 = H$  (**b**);  $R^1 = H, R^2 = i\text{-Bu}$  (**c**), **Me** (**d**), **Pr** (**e**); **III**,  $R^3 = H, R^4 = PhCH_2$ ; **IV**,  $R^3R^4N = \text{morpholino}$ ; **V**,  $R^3R^4N = \text{pyrrolidin-1-yl}$ ; **VI**,  $R^3R^4N = \text{piperidino}$ ; **VII**,  $R^3 = H, R^4 = 4\text{-MeOC}_6\text{H}_4$ ; **VIII**,  $R^3 = H, R^4 = \text{naphthalen-1-yl}$ .

Scheme 2.



**IX, X**,  $R^3R^4N = \text{morpholino}$  (**a**), **pyrrolidin-1-yl** (**b**), **piperidino** (**c**).

group exhibit biological activity or are used as medicines [9, 10]. It is also known [11–13] that opening of the oxirane ring by the action of nucleophiles follows Krasuskii rule provided that electronegative substituent (*-I*) is present at the oxirane ring.

With a view to obtain new  $\beta$ -amino alcohol derivatives as potential biologically active substances, 4-(2,3-epoxypropoxy)-2*H*-chromen-2-ones **IIa–IIe** were brought into reaction with benzylamine, 1-naphthylamine, *p*-anisidine, piperidine, pyrrolidine, and morpholine. The optimal reaction conditions were as follows: reactant molar ratio (**II**–amine) 1:1.5, solvent dioxane, temperature 85–90°C, reaction time 6 h. The products were the corresponding amino alcohols **III–VIII** (Scheme 1) whose structure was confirmed by elemental analyses and spectral data. Amino alcohols **IVa–VIa** were treated with benzoyl chloride, and benzoate hydrochlorides **IXa–IXc** thus formed were converted into free bases **Xa–Xc** by the action of aqueous ammonia (Scheme 2).

## EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer from samples dispersed in mineral oil. The  $^1\text{H}$  NMR spectra were measured on a Tesla BS-497 instrument (100 MHz) from solutions in  $\text{CDCl}_3$  using hexamethyldisiloxane as internal reference.

**4-(2,3-Epoxypropoxy)-2*H*-chromen-2-one (IIa).** A mixture of 3.24 g (20 mmol) of 4-hydroxy-2*H*-chromen-2-one (**Ia**), 28 g (20 mmol) of potassium carbonate, and 1.9 ml (30 mmol) of 2-chloromethyl-oxirane in 3 ml of acetone was heated for 5 h at 70°C. The mixture was cooled, diluted with water, and extracted with diethyl ether. The extract was evaporated, and the residue was recrystallized from aqueous alcohol (1:1). Yield 3.4 g (78%), colorless crystals, mp 162°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1725 (C=O), 1610, 1565, 1525 (C=C<sub>arom</sub>), 1250, 1020, 840 (oxirane).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 6.8–7.0 m (4H, H<sub>arom</sub>), 5.8 s (1H, CH), 2.95 m (1H, CH), 2.35–2.65 m (4H, CH<sub>2</sub>). Found, %: C 65.75; H 4.61.  $\text{C}_{12}\text{H}_{10}\text{O}_4$ . Calculated, %: C 66.00; H 4.59.

Compounds **IIb–IIe** were synthesized in a similar way.

**4-(2,3-Epoxypropoxy)-5-methyl-2*H*-chromen-2-one (IIb).** Yield 3.53 g (76%), mp 174°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1725 (C=O), 1620 (C=C), 1250, 1015, 840 (oxirane). Found, %: C 67.52; H 5.21.  $\text{C}_{13}\text{H}_{12}\text{O}_4$ . Calculated, %: C 67.24; H 6.57.

**4-(2,3-Epoxypropoxy)-3-isobutyl-2*H*-chromen-2-one (IIc).** Yield 4.1 g (74%), mp 172°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1720 (C=O), 1615 (C=C<sub>arom</sub>), 1250, 1010, 835 (oxirane). Found, %: C 71.05; H 6.75.  $\text{C}_{16}\text{H}_{18}\text{O}_4$ . Calculated, %: C 70.73; H 6.57.

**4-(2,3-Epoxypropoxy)-3-methyl-2*H*-chromen-2-one (IIId).** Yield 3.32 g (72%), mp 169°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1720 (C=O), 1620 (C=C), 1250, 1010, 840 (oxirane). Found, %: C 67.32; H 6.41.  $\text{C}_{13}\text{H}_{12}\text{O}_4$ . Calculated, %: C 67.24; H 6.57.

**4-(2,3-Epoxypropoxy)-3-propyl-2*H*-chromen-2-one (IIe).** Yield 3.66 g (71%), mp 164°C. Found, %: C 68.97; H 6.05.  $\text{C}_{15}\text{H}_{16}\text{O}_4$ . Calculated, %: C 69.23; H 6.15.

**4-(3-Benzylamino-2-hydroxypropoxy)-2*H*-chromen-2-one (IIIa).** A mixture of 2.18 g (10 mmol) of compound **IIa**, 1.16 (10 mmol) of freshly distilled benzylamine, and 10 ml of dioxane was heated for 6 h at 89–90°C. The solvent was removed under reduced pressure, and the residue was washed with hexane and recrystallized from chloroform–petroleum ether (1:1). Yield 2.6 g (80%), mp 183°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3520 (NH), 3240 (OH), 1720 (C=O), 1610 (C=C), 1245 (C–O–C).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 7.60–8.05 m (4H, H<sub>arom</sub>), 7.20 (3H, H<sub>arom</sub>,  $J = 7.2$  Hz), 6.95 (2H, H<sub>arom</sub>,  $J = 8.5$  Hz), 5.80 (1H, CH), 4.30 m (CHOH), 3.95 d (1H, OCH<sub>2</sub>,  $J = 4.5$  Hz), 3.80 d (2H, CH<sub>2</sub>Ph,  $J = 12.8$  Hz), 3.75 d (1H, OCH<sub>2</sub>,  $J = 3.5$  Hz), 3.50 m (2H, NH, OH), 2.75 d.d (1H, CH<sub>2</sub>N,  $J = 7.5$ , 12.8 Hz), 2.60 d.d (1H, CH<sub>2</sub>N,  $J = 7.5$ , 12.8 Hz). Found, %: C 70.25; H 5.62; N 4.25.  $\text{C}_{19}\text{H}_{19}\text{NO}_4$ . Calculated, %: C 70.15; H 5.85; N 4.31.

Compounds **IIIb–IIIe**, **IVa–IVe**, **Va–Ve**, **VIa–VIe**, **VIIa–VIIe**, and **VIIIa–IIIe** were synthesized in a similar way.

**4-(3-Benzylamino-2-hydroxypropoxy)-5-methyl-2*H*-chromen-2-one (IIIb).** Yield 2.64 g (78%), mp 185–186°C (from  $\text{CHCl}_3$ ). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3420 (NH), 3240 (OH), 1720 (C=O), 1610 (C=C), 1260. Found, %: C 71.05; H 6.21; N 4.21.  $\text{C}_{20}\text{H}_{21}\text{NO}_4$ . Calculated, %: C 70.796; H 6.195; N 4.130.

**4-(3-Benzylamino-2-hydroxypropoxy)-3-isobutyl-2*H*-chromen-2-one (IIIc).** Yield 2.8 g (75%), mp 173–174°C (from  $\text{CHCl}_3$ ). Found, %: C 71.95; H 7.13; N 3.71.  $\text{C}_{23}\text{H}_{27}\text{NO}_4$ . Calculated, %: C 72.44; H 7.09; N 3.675.

**4-(3-Benzylamino-2-hydroxypropoxy)-3-methyl-2*H*-chromen-2-one (IIIId).** Yield 2.65 g (79%), mp 189–190°C (from  $\text{CHCl}_3$ ). Found, %: C 70.87;

H 6.05; N 4.23. C<sub>20</sub>H<sub>21</sub>NO<sub>4</sub>. Calculated, %: C 70.96; H 6.19; N 4.13.

**4-(3-Benzylamino-2-hydroxypropoxy)-3-propyl-2H-chromen-2-one (IIIe).** Yield 2.7 g (74%), mp 166–167°C (from CHCl<sub>3</sub>). Found, %: C 71.81; H 6.73; N 3.49. C<sub>22</sub>H<sub>25</sub>NO<sub>4</sub>. Calculated, %: C 71.94; H 6.81; N 3.82.

**4-(2-Hydroxy-3-morpholinopropoxy)-2H-chromen-2-one (IVa).** Yield 2.35 g (77%), mp 191°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3245 (OH), 1720 (C=O), 1620, 1560, 1525 (C=C<sub>arom</sub>), 1240 (COC). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.40–8.15 m (4H, H<sub>arom</sub>), 5.70 s (1H, CH), 4.80 br.s (1H, OH), 4.10 m (2H, OCH<sub>2</sub>, CHOH), 4.00 m (1H, OCH<sub>2</sub>, *J* = 3.5 Hz), 3.60 m (4H, CH<sub>2</sub>OCH<sub>2</sub>), 2.65 d (2H, NCH<sub>2</sub>, *J* = 7.6 Hz), 2.28 m (4H, CH<sub>2</sub>NCH<sub>2</sub>). Found, %: C 62.4; H 6.50; N 4.25. C<sub>16</sub>H<sub>19</sub>NO<sub>5</sub>. Calculated, %: C 62.95; H 6.23; N 4.59.

**4-(2-Hydroxy-3-morpholinopropoxy)-5-methyl-2H-chromen-2-one (IVb).** Yield 2.47 g (74%), mp 187–188°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 63.3; H 6.25; N 4.16. C<sub>17</sub>H<sub>21</sub>NO<sub>5</sub>. Calculated, %: C 63.95; H 6.58; N 4.39.

**4-(2-Hydroxy-3-morpholinopropoxy)-3-isobutyl-2H-chromen-2-one (IVc).** Yield 2.62 g (73%), mp 179–180°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 67.10; H 7.25; N 3.67. C<sub>20</sub>H<sub>27</sub>NO<sub>5</sub>. Calculated, %: C 66.48; H 7.48; N 3.88.

**4-(2-Hydroxy-3-morpholinopropoxy)-3-methyl-2H-chromen-2-one (IVd).** Yield 2.41 g (76%), mp 157–158°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 63.15; H 6.22; N 4.31. C<sub>17</sub>H<sub>21</sub>NO<sub>5</sub>. Calculated, %: C 63.95; H 6.58; N 4.39.

**4-(2-Hydroxy-3-morpholinopropoxy)-3-propyl-2H-chromen-2-one (IVe).** Yield 2.47 g (71%), mp 144–145°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 65.47; H 7.31; N 4.17. C<sub>19</sub>H<sub>25</sub>NO<sub>5</sub>. Calculated, %: C 65.71; H 7.20; N 4.035.

**4-[2-Hydroxy-3-(pyrrolidin-1-yl)propoxy]-2H-chromen-2-one (Va).** Yield 2.1 g (71%), mp 175°C (from CCl<sub>4</sub>–petroleum ether, 2:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3260 (OH), 1720 (C=O), 1620, 1565, 1520 (C=C<sub>arom</sub>), 1250 (COC). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.6–7.9 m (4H, H<sub>arom</sub>), 5.75 s (1H, CH), 4.80 br.s (1H, OH), 4.20 m (2H, OCH<sub>2</sub>, CHOH), 3.68 d (1H, OCH<sub>2</sub>, *J* = 3.6 Hz), 2.54 m (4H, CH<sub>2</sub>CH<sub>2</sub>), 2.42 d.d (1H, NCH<sub>2</sub>, *J* = 7.7, 12.6 Hz), 1.82 m (4H, CH<sub>2</sub>NCH<sub>2</sub>). Found, %: C 66.20; H 6.45; N 4.25. C<sub>16</sub>H<sub>19</sub>NO<sub>4</sub>. Calculated, %: C 66.44; H 6.57; N 4.84.

**4-[2-Hydroxy-3-(pyrrolidin-1-yl)propoxy]-5-methyl-2H-chromen-2-one (Vb).** Yield 2 g (68%), mp 169°C (from CCl<sub>4</sub>–petroleum ether, 2:1). Found, %: C 67.52; H 7.01; N 4.58. C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>. Calculated, %: C 67.33; H 6.93; N 4.62.

**4-[2-Hydroxy-3-(pyrrolidin-1-yl)propoxy]-3-isobutyl-2H-chromen-2-one (Vc).** Yield 2.3 g (65%), mp 192–193°C (from CCl<sub>4</sub>–petroleum ether, 2:1). Found, %: C 69.32; H 7.64; N 4.17. C<sub>20</sub>H<sub>27</sub>NO<sub>4</sub>. Calculated, %: C 69.57; H 7.83; N 4.06.

**4-[2-Hydroxy-3-(pyrrolidin-1-yl)propoxy]-3-methyl-2H-chromen-2-one (Vd).** Yield 1.87 g (64%), mp 136–137°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 67.15; H 6.87; N 4.70. C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>. Calculated, %: C 67.33; H 6.93; N 4.62.

**4-[2-Hydroxy-3-(pyrrolidin-1-yl)propoxy]-3-propyl-2H-chromen-2-one (Ve).** Yield 2.13 g (65%), mp 129–130°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 69.10; H 7.73; N 4.35. C<sub>19</sub>H<sub>25</sub>NO<sub>4</sub>. Calculated, %: C 68.88; H 7.55; N 4.23.

**4-(2-Hydroxy-3-piperidinopropoxy)-2H-chromen-2-one (VIa).** Yield 2.24 g (74%), mp 167°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3260 (OH), 1720 (C=O), 1620, 1560, 1520 (C=C<sub>arom</sub>), 1240 (COC). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.70–8.10 m (4H, H<sub>arom</sub>), 5.82 s (1H, CH), 4.85 br.s (1H, OH), 4.25 m (2H, OCH<sub>2</sub>, CHOH), 3.80 d (1H, OCH<sub>2</sub>, *J* = 3.5 Hz), 2.6 d.d (1H, NCH<sub>2</sub>, *J* = 8.2, 12.7 Hz), 2.4 d.d (1H, NCH<sub>2</sub>, *J* = 8.2, 12.7 Hz), 2.15 m (4H, CH<sub>2</sub>NCH<sub>2</sub>), 1.32 m (6H, CH<sub>2</sub>). Found, %: C 67.25; H 7.02; N 4.58. C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>. Calculated, %: C 67.33; H 6.93; N 4.62.

**4-(2-Hydroxy-3-piperidinopropoxy)-5-methyl-2H-chromen-2-one (VIb).** Yield 2.28 g (72%), mp 176°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 68.27; H 7.14; N 4.51. C<sub>18</sub>H<sub>23</sub>NO<sub>4</sub>. Calculated, %: C 68.14; H 7.26; N 4.42.

**4-(2-Hydroxy-3-piperidinopropoxy)-3-isobutyl-2H-chromen-2-one (VIc).** Yield 2.3 g (64%), mp 182°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 70.22; H 8.10; N 3.71. C<sub>21</sub>H<sub>29</sub>NO<sub>4</sub>. Calculated, %: C 70.19; H 8.08; N 3.89.

**4-(2-Hydroxy-3-piperidinopropoxy)-3-methyl-2H-chromen-2-one (VIId).** Yield 2.2 g (70%), mp 174–175°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 68.14; H 7.26; N 4.51. C<sub>18</sub>H<sub>23</sub>NO<sub>4</sub>. Calculated, %: C 68.14; H 7.26; N 4.42.

**4-(2-Hydroxy-3-piperidinopropoxy)-3-propyl-2H-chromen-2-one (VIe).** Yield 2.17 g (63%),

mp 167–168°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). Found, %: C 69.63; H 7.49; N 4.11. C<sub>20</sub>H<sub>27</sub>NO<sub>4</sub>. Calculated, %: C 69.56; H 7.89; N 4.06.

**4-[2-Hydroxy-3-(4-methoxyphenylamino)propoxy]-2H-chromen-2-one (VIIa).** Yield 2.18 g (67%), mp 187–188°C. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3520 (NH), 3445 (OH), 3030 (C–H<sub>arom</sub>), 1720 (C=O), 1610 (C=C<sub>arom</sub>), 1580 ( $\delta$ NH), 1250 (COC). Found, %: C 70.34; H 5.67; N 4.25. C<sub>19</sub>H<sub>19</sub>NO<sub>5</sub>. Calculated, %: C 66.86; H 5.57; N 4.11.

**4-[2-Hydroxy-3-(4-methoxyphenylamino)propoxy]-5-methyl-2H-chromen-2-one (VIIb).** Yield 2.25 g (67%), mp 201–202°C. Found, %: C 67.50; H 5.31; N 3.52. C<sub>20</sub>H<sub>21</sub>NO<sub>5</sub>. Calculated, %: C 67.61; H 5.92; N 3.94.

**4-[2-Hydroxy-3-(4-methoxyphenylamino)propoxy]-3-isobutyl-2H-chromen-2-one (VIIc).** Yield 2.61 g (69%), mp 197–198°C. Found, %: C 69.56; H 6.98; N 3.61. C<sub>23</sub>H<sub>27</sub>NO<sub>5</sub>. Calculated, %: C 69.52; H 6.80; N 3.53.

**4-[2-Hydroxy-3-(4-methoxyphenylamino)propoxy]-3-methyl-2H-chromen-2-one (VIIId).** Yield 2.19 g (65%), mp 204–205°C. Found, %: C 67.86; H 5.75; N 3.47. C<sub>20</sub>H<sub>21</sub>NO<sub>5</sub>. Calculated, %: C 67.61; H 5.92; N 3.94.

**4-[2-Hydroxy-3-(4-methoxyphenylamino)propoxy]-3-propyl-2H-chromen-2-one (VIIe).** Yield 2.39 g (65%), mp 183–184°C. Found, %: C 68.60; H 7.05; N 3.75. C<sub>22</sub>H<sub>25</sub>NO<sub>5</sub>. Calculated, %: C 68.93; H 6.53; N 3.66.

**4-[2-Hydroxy-3-(naphthalen-1-ylamino)propoxy]-2H-chromen-2-one (VIIIa).** Yield 2.92 g (81%), mp 213–214°C (from CHCl<sub>3</sub>–petroleum ether, 1:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3460 (OH), 3230 (NH), 3030 (C–H<sub>arom</sub>), 1720 (C=O), 1620 (C=C<sub>arom</sub>), 1610 (C=C<sub>arom</sub>), 1580 ( $\delta$ NH), 1245 (COC). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.85 t (2H, NCH<sub>2</sub>, *J* = 7.5 Hz), 4.25 d (1H, OCH<sub>2</sub>, *J* = 5.7 Hz), 4.35 m (1H, CHOH), 4.85 d (1H, OH), 7.3–8.05 m (10H, H<sub>arom</sub>), 7.20 d (1H, H<sub>arom</sub>), 7.00 d (1H, H<sub>arom</sub>). Found, %: C 73.26; H 5.32; N 4.05. C<sub>22</sub>H<sub>19</sub>NO<sub>4</sub>. Calculated, %: C 73.13; H 5.26; N 3.88.

**4-[2-Hydroxy-3-(naphthalen-1-ylamino)propoxy]-5-methyl-2H-chromen-2-one (VIIIb).** Yield 3.1 g (82%), mp 222–223°C. Found, %: C 73.25; H 5.71; N 3.84. C<sub>23</sub>H<sub>21</sub>NO<sub>4</sub>. Calculated, %: C 73.60; H 5.60; N 3.73.

**4-[2-Hydroxy-3-(naphthalen-1-ylamino)propoxy]-3-isobutyl-2H-chromen-2-one (VIIIc).** Yield 3.48 g (84%), mp 207–208°C. Found, %: C 75.00;

H 6.59; N 3.45. C<sub>26</sub>H<sub>27</sub>NO<sub>4</sub>. Calculated, %: C 74.82; H 6.47; N 3.36.

**4-[2-Hydroxy-3-(naphthalen-1-ylamino)propoxy]-3-methyl-2H-chromen-2-one (VIIId).** Yield 3.1 g (82%), mp 225–226°C. Found, %: C 73.45; H 5.32; N 4.38. C<sub>23</sub>H<sub>21</sub>O<sub>4</sub>N. Calculated, %: C 73.60; H 5.60; N 3.73.

**4-[2-Hydroxy-3-(naphthalen-1-ylamino)propoxy]-3-propyl-2H-chromen-2-one (VIIIe).** Yield 3.6 g (84%), mp 210–211°C. Found, %: C 74.64; H 6.38; N 3.64. C<sub>25</sub>H<sub>25</sub>O<sub>4</sub>N. Calculated, %: C 74.44; H 6.20; N 3.47.

**4-[2-Benzoyloxy-3-(2-oxo-2H-chromen-4-yloxy)propyl]morpholin-4-ium chloride (IXa).** A mixture of 4 g (13 mmol) of compound IVa and 1.83 g (13 mmol) of benzoyl chloride in 5 ml of toluene was kept for 15–20 h at room temperature and was then heated for 3 h at 90–95°C. The mixture was cooled, and the precipitate was filtered off, washed with diethyl ether, and dried. Yield 5.45 g (93%), mp 289–291°C. Found, %: C 62.05; H 5.27; Cl 7.79; N 3.21. C<sub>23</sub>H<sub>23</sub>NO<sub>6</sub>·HCl. Calculated, %: C 61.95; H 5.39; Cl 7.97; N 3.14.

Compounds IXb and IXc were synthesized in a similar way.

**1-[2-Benzoyloxy-3-(2-oxo-2H-chromen-4-yloxy)propyl]pyrrolidinium chloride (IXb).** Yield 5.16 g (93%), mp 285–287°C. Found, %: C 64.31; H 5.48; Cl 8.39; N 3.17. C<sub>23</sub>H<sub>23</sub>NO<sub>5</sub>·HCl. Calculated, %: C 64.26; H 5.36; Cl 8.27; N 3.26.

**1-[2-Benzoyloxy-3-(2-oxo-2H-chromen-4-yloxy)propyl]piperidinium chloride (IXc).** Yield 5.45 g (95%), mp 297–299°C. Found, %: C 65.01; H 5.78; Cl 7.96; N 3.22. C<sub>24</sub>H<sub>25</sub>NO<sub>5</sub>·HCl. Calculated, %: C 64.94; H 5.86; Cl 8.00; N 3.16.

**2-Morpholino-1-[(2-oxo-2H-chromen-4-yloxy)methyl]ethyl benzoate (Xa).** A suspension of compound IXa in 3 ml of benzene was treated with an ammonia solution to attain pH 10. The precipitate was filtered off, dried, and recrystallized from chloroform–petroleum ether (1:1). Yield 3.37 g (83%), mp 212–213°C. IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3035 (C–H<sub>arom</sub>), 1745 (C=O, ester), 1720 (C=O, lactone), 1620, 1560, 1530 (C=C<sub>arom</sub>), 1245 (COC). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.30–7.52 m (5H, H<sub>arom</sub>), 6.90–7.20 m (4H, H<sub>arom</sub>), 5.9 s (1H, CH), 3.90 m (3H, CH<sub>2</sub>O, CHO), 3.60 m (4H, CH<sub>2</sub>OCH<sub>2</sub>), 2.68 m (6H, CH<sub>2</sub>N). Found, %: C 67.53; H 5.69; N 3.22. C<sub>23</sub>H<sub>23</sub>NO<sub>6</sub>. Calculated, %: C 67.48; H 5.62; N 3.42.



Compounds **Xb** and **Xc** were synthesized in a similar way.

**1-[2-Oxo-2H-chromen-4-yloxy)methyl]-2-(pyrrolidin-1-yl)ethyl benzoate (Xb)**. Yield 3.3 g (84%), mp 201–202°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3030 (C–H<sub>arom</sub>), 1740 (C=O, ester), 1720 (C=O, lactone), 1625, 1560, 1525 (C=C<sub>arom</sub>), 1250 (COC). Found, %: C 70.41; H 5.69; N 3.43. C<sub>23</sub>H<sub>23</sub>NO<sub>5</sub>. Calculated, %: C 70.23; H 5.85; N 3.56.

**1-[2-Oxo-2H-chromen-4-yloxy)methyl]-2-piperidinoethyl benzoate (Xc)**. Yield 3.47 g (85%), mp 185–186°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.50–7.30 m (5H, H<sub>arom</sub>), 6.97–7.10 m (4H, H<sub>arom</sub>), 5.82 s (1H, CH), 3.85 m (3H, CH<sub>2</sub>O, CHO), 2.30 m (6H, CH<sub>2</sub>N), 1.50 m (4H, CH<sub>2</sub>), 1.40 m (2H, CH<sub>2</sub>). Found, %: C 70.43; H 6.27; N 3.61. C<sub>24</sub>H<sub>25</sub>NO<sub>5</sub>. Calculated, %: C 70.76; H 6.14; N 3.44.

#### REFERENCES

1. Avetisyan, A.A. and Alvandzhyan, A.G., *Russ. J. Org. Chem.*, 2006, vol. 42, p. 1063.
2. Bergmeier, S.C., *Tetrahedron*, 2000, vol. 56, p. 2561.
3. Karpf, M. and Trussardi, R.J., *J. Org. Chem.*, 2001, vol. 66, p. 2044.
4. Inaba, T., Yamada, Y., Abe, H., Sagawa, S., and Cho, H., *J. Org. Chem.*, 2000, vol. 65, p. 1623.
5. Cristau, H.J., Pirat, J.L., Drag, M., and Kafarski, P., *Tetrahedron Lett.*, 2000, vol. 41, p. 9781.
6. Hudlicky, T., Abbod, K.F., Entwisle, D.A., Fan, R., Maurya, R., Thorpe, A.J., Bolonick, J., and Myers, B., *Synthesis*, 1996, no. 7, p. 897.
7. FRG Patent Appl. no. 19724186, 1998; *Ref. Zh., Khim.*, 2002, no. 19O116P.
8. Sabitha, G., Babu, R.S., Rajkumar, M., and Yadav, J.S., *Org. Lett.*, 2002, vol. 4, p. 343.
9. Mashkovskii, M.D., *Lekarstvennye sredstva (Drugs)*, Moscow: Novaya Volna, 2002, vol. 1, pp. 253, 368, 385; vol. 2, pp. 295, 303, 362.
10. Lukevits, E.Ya., Libert, L.I., and Voronkov, M.G., *Usp. Khim.*, 1970, vol. 39, p. 2005.
11. Mislyuk, O.A., Shibaev, V.I., Davidenkov, L.R., Vyunov, K.A., and Ginak, A.I., *Zh. Prikl. Khim.*, 1984, vol. 57, p. 2138.
12. Mislyuk, O.A., Shibaev, V.I., Vyunov, K.A., and Ginak, A.I., *Zh. Org. Khim.*, 1986, vol. 22, p. 2227.
13. Vladimirov, M.G. and Petrov, A.A., *Zh. Obshch. Khim.*, 1947, vol. 17, p. 51.